

2024 CDISC + TMF PHOENIX/SCOTTSDALE

23-24 OCTOBER: CONFERENCE & EXPO | 21, 22, 25 OCTOBER: TRAININGS



FDA business rules and CDISC Open Rules, the road to adoption

Nick De Donder, CDISC Open Rules Program Manager, CDISC



Meet the Speaker

Nick De Donder

Title: CDISC Open Rules Program Manager

Organization: CDISC

Nick De Donder graduated as a biomedical scientist from the University of Ghent, Belgium in 2007 and has been employed since 2008 by Business & Decision Life Sciences at their headquarters in Brussels. He has been moving from being a Data Integration Specialist to Project Manager to Line Manager for the Data Standards team. Since 2020 he is Head of Data Standards. Nick is a member of the SDS team, an authorized CDISC trainer for CDASH, SDTM and Newcomers and a PHUSE committee member since 2017. In 2019 he joined the E3C and is now cochairing it. Since June 2021 Nick has been program manager of the CDISC Open Rules project.

Agenda

- 1. Research Collaboration Agreement
- 2. FDA Business Rules
- 3. Into Practice
- 4. Progress
- 5. Next Steps

What are CDISC Open Rules?





- Rules: Complete set of aligned, open and unambiguous machine-readable conformance rules for each standard including CDISC, Regulatory, and Industry needs
- **Governance:** Well-defined governance model for the evaluation, development, and publication of rules from all stakeholders
- Engine: Open-source rules engine available for testing and community use

FDA Business Rules



Background

- Sponsors should evaluate their study data before submission against the conformance rules published by an SDO, the eCTD Technical Rejection Criteria for Study Data, and the FDA Business Rules.
- The Business Rules v1.5 (May 2019) help ensure that the study data are compliant, useful, and will support meaningful review and analysis. This applies to SDTM formatted clinical studies and SEND formatted non-clinical studies. For more information, see Section 8 of the Technical Conformance Guide.
- All business rules should be followed where applicable.



Research Collaboration Agreement with US FDA CDER & CBER

In LLS. Find and Daug Administration's Office of Translational Sciences in the Contention (ang Evaluation and Research and Office of Regulatory Operations in the Center for Resigns Evaluation and Research to Incorporate FOA Basiness Rains into (2018/CS Open Failes Logine (2014).

SDIRCS CODE project previous an approvisional version of the CDIRC Conference basis is a machine executable tomail. These cases sublished and managed by CDIRC, oreale a large source for confermance name and allow extendition and sponsor companies to replement, and extend these cases within thes hows. <u>TCR Doctores Rates</u> are correctly within in a pain tool, sov-machine consultate formal and doctorie the business equiprements for regulatory writes to region and concurring shall do a in completed indicated and supports moving for soview and assigns.

tastin, TX - January 15, 2024 - CDSC a talk of their elements a research collaboration with

The goal of this effort, which began on November 3, 2002 and Sas term of Twee years, is to instancests on providing input on machine-oversidable formation of the FCA Business Rains and on the development and origing governments allities set of executable rules within CORE fait rate the asset the serverees of earlier to reveal adverse.

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the lot Next Ne	
342008	Altmainent operare date inte sheald its between fast and last study taxament date inte
342009	Alpaint variable deult have a one-to-ore relationship. Stamples incluit elent same and name offent parameter name and parameter orde or number, variable nam and variable label, etc.
348011	Altrial design data shevid be silvetited as specified in the FDA. Study Data Technical Confirmance Guide (TCG).
342012	Deverand in v1.5.
M2013	Devez and in vil 3.
342015	Claracter values insident have lader managements in east resid claracter.
10R016	Collection and a family for several of show for Heart Production is analyhic
348017	Completioners should at the countermicate, speling and purchasing and by the tempology maintenance organizations (e.g., ModSRA, CDS Constrolled tempology).
AB018	A variable's length access a study should be no lenger than the maximum length office actual data (expect for \$7,790 (241)
348019	5.790 U.L. valable length level to me langer than the maximum length of the actual

CDISC and FDA working together to develop machine-executable formats of the FDA Business Rules and on the development and ongoing governance of this set of executable rules within the CDISC Open Rules project that can be used by industry

The benefits of creating a single source of truth for all FDA validation needs increases transparency for all stakeholders on how FDA checks data for conformance to CDISC standards and to existing FDA Business Rules





Into Practice

FDA Business Rules

FDA Business Rule ID	FDA Business Rule	
Clinical and Nonclinical	(SDTMIG, SEND)	
FDAB008	All treatment exposure date/time should be between first and last study treatment	
	date/time.	Ru
FDAB009	All paired variables should have a one-to-one relationship. Examples include short	
	name and name of test; parameter name and parameter code or number; variable name	
	and variable label, etc.	
FDAB011	All trial design data should be submitted as specified in the FDA Study Data Technical	
	Conformance Guide (TCG).	FB08
FDAB015	Character values should not have leading spaces or only have a period character.	
FDAB016	Collection study day should be populated when date/time of collection is available.	FB09
FDAB017	Controlled terms should use the exact term (case, spelling, and punctuation) used by	
	the terminology maintenance organizations (e.g., MedDRA, CDISC controlled	
	terminology).	FB09
FDAB018	A variable's length across a study should be no longer than the maximum length of the	
	actual data (except for SUPPQUAL).	
FDAB019	SUPPQUAL variable length should be no longer than the maximum length of the actual	FB09
	data within the dataset.	FBU9
FDAB024	Large datasets should be split into smaller datasets no larger than 5 GB in size.	
FDAB026	Records with a baseline flag should have a corresponding standard result with a	FB09
	standardized unit where available.	
FDAB030	Standard units should be consistent within the same assessment (having the same	
	TESTCD,CAT,SCAT,SPEC,METHOD values).	FB09
	1	FB09

	Ident	ifiers				Scope o	f Rule		
Rule ID .T	Rule ID Version (represents any change to the rule)	Related Rule(s) [See Also, Compare Against ¥	Rule Set (Generally IG Version, OCCDS v1.0, ADNCA v1	Class 💌	Subclass 🗸	Dataset or Domai	Variable	Elemen 🔻	Scope Section 🗸
						EC, EX (merged	STDTC,ENDTC, RFXSTDTC,	ltemGroup Def	
FB0801	1			INT		w/DM)	RFXENDTC	ItemDef	
FB0901	1		All SDTMIG, SENDIG	ALL		ALL	Variable name and variable label		
FB0902	1		All SDTMIG, SENDIG	FND, TDM		All	TESTCD, TEST		
FB0903	1		Ali SDTMIG, SENDIG	SPC, TDM		DM, TA, TV, TE	DM.ARM-DM.ARMCD, DM.ACTARM-DM.ACTARMCD, TA.ARM-TA.ARMCD, TA.ACTARM-TA.ACTARMCD, TV.ARM-TV.ARMCD, TV.ACTARM-TV.ACTARMCD, TE.ELEMENT-TE.ETCD		
FB0904	1		All SDTMIG, SENDIG	TDM		TS	TS.TSVAL-TS.TSVALCD- TS.TSVALNF		
FB0905	1		All SDTMIG	INT		AG, CM, SU	CLAS,CLASCD		
FB0910	1		All SDTMIG	TDM		ті	TI.IETEST, TI.IETESTCD		





Harmonized spreadsheet

	Identi	fiers					Release Notes	
) (re an		Compare	Rule Set (Generally IG Version, OCCDS v1.0, ADNCA v1 🔻	Scope Sectior 🔻	Rule Sectic •	Guidance Section 💌	Release Notes	Authoring



Business specification

Ve (rep any	Rule ID /ersion presents y change the rule)		Rule Set (Generally IG Version, OCCDS v1.0, ADNCA v1 💌	Scope Section	Natural Language Pulo							
Rule ID -T	•	Against	ADNCA v1 -		Natural Language Rule			Natural Language Rule (Failure				
				Jecuol	(Success Criteria)	Rule (Success Criteria)	Condition (Success) Variables exists and are	Criteria)	Rule (Failure Criteria) 🔻	Condition (Failure)	Error Message	- Executabili -
							populated; otherwise, account for all possibilities and treat					
					All treatment exposure		with ANY conditions. Note: need functionality 'check for RFXDTC availability in IG'					
					date/time should be		for generic rule			Variables exists and populated;		
					between first and last		implementation. Note: NA for	All treatment exposure		otherwise, account for all	All treatment exposure date/time	
					study treatment	(RFXSTDTC <=STDTC <=ENDTC	earlier SENDIGs that don't have	date/time outside first and last	not (RFXSTDTC <=STDTC	possibilities and treat with ANY	outside first and last study	Fully
FB0801	1				date/time.	<= RFXENDTC	RFXDTC.	study treatment date/time.	<= ENDTC <= RFXENDTC)	conditions.	treatment date/time.	executable
			All SDTMIG,					One-to-one mapping is not	Variable name and label		One-to-one mapping is not	Fully
FB0901	1		SENDIG			One-to-one		maintained.	pairing is not unique		maintained.	executable
					TESTCD and TEST pair							
FB0902	1		All SDTMIG, SENDIG		should have one-to-one relationship	One-to-one		One-to-one mapping is not maintained.	Pairing is not unique		One-to-one mapping is not maintained.	Fully executable
			All SDTMIG,					One-to-one mapping is not			One-to-one mapping is not	Fully
FB0903	1		SENDIG			One-to-one		maintained.	Pairing is not unique		maintained.	executable
											0	Fully.
FB0904	1		All SDTMIG, SENDIG			One-to-one	TSVALCD ^= null	One-to-one mapping is not maintained.	Pairing is not unique		One-to-one mapping is not maintained.	Fully executable
100304	1		SCINDIG			one-to-one	ISVALOU HUII	mantaneu.	ranng is not unique		mantanleu.	evecutable
								One-to-one mapping is not			One-to-one mapping is not	Fully
FB0905	1		All SDTMIG			One-to-one		maintained.	Pairing is not unique		maintained.	executable
												For Here
FB0910	1		All SDTMIG			One-to-one		One-to-one mapping is not maintained.	Pairing is not unique		One-to-one mapping is not maintained.	Fully executable



Business rule to executability

FDAB036 The value for study day should not be negative for exposure treatments.

•••		Ident	ifiers					S					
		Rule ID Version (represents any change to the rule)	[See Also, Compare	Rule Set (Generally IG Version, OCCDS v1.0, ADNCA v1 🗸	Scope Sectioi ▼	Natural Language Rule (Success Criteria) 💌 Rule (Success C	riteria) 💌 Condi	ition (Success) 💌	Natural Language Rule (Failure Criteria)	▼ Rule (Failure Criteria) ▼	Condition (Failure)	Error Message	 Executabili •
						The value for study day			The value for study day is				
						should not be negative for			negative for exposure				Fully
1	FB3601	1				exposure treatmentsSTDY > 0 andENDY	>0	1	reatments.	STDY < 0 orENDY < 0			executable
				€ ✓ Det	FB360	es / CORERULES-9240 D1 Id comment Assign More v Published v				value: 0 - name:	: less_than ENDY : less_than)		
				Тур	e:	Review Comments	Resolution: U	nresolved		Status: Publ			
				Prio	ority:	To be assigned	Fix Version/s: N	lone		Version: '1'			
				Affe	ects Version/	-				Description: S (EC/EX) data	study Day variables (DY) value s	hould not be negative in Exposur	'e
				Con	nponent/s:	FDA SDTMIG v3.2, FDA SDTMIG v3.3,					Fully Executable		
						FDA SDTMIG v3.4, FDA SENDIG DART				Outcome:			
						v1.1, FDA SENDIG DART v1.2, FDA				Message: Neg Output Varia	ative value of Study Day variable		
						SENDIG GENETOX v1.0, FDA SENDIG v3.0, FDA SENDIG v3.1, FDA SENDIG				STDY	bles:		
						v3.1.1, FDA SENDIG-AR v1.0 ···				ENDY			
1				Lab	els:	None				Rule Type: Rec	ord Data		
				Exe	cutability:	Fully Executable				Scope: Classes:			
										Include:			
				✓ Des	scription					Domains:			
				Na	atural Langua	age Rule (Success Criteria)	Rule (Success Criteria)	Condition (Success)		Include:			
						tudy day should not be negative for exposure treatmen	tsSTDY > 0 andENDY >			- EC - EX			
		1.						1		Sensitivity: R			





Test data

Positive test data does not show issues

EPOCH	Ŧ	EXSTDTC	-	EXENDTC	Ŧ	EXSTDY	EXENDY
		Start Date/Time of		End Date/Time of		Study Day of Start of	Study Day of End of
Epoch		Treatment		Treatment		Treatment	Treatment
Char		Char		Char		Num	Num
50		50		50		8	8
TREATMENT		2012-12-01		2012-12-01		2	2
TREATMENT		2012-12-02		2012-12-02		0	3
TREATMENT		2012-12-03		2012-12-03		4	4
TREATMENT		2012-11-30		2012-11-30		1	1

• Negative test data contains issues

EPOCH	Ŧ	EXSTDTC	Ŧ	EXENDTC	Ŧ	EXSTDY	Ŧ	EXENDY	-
		Start Date/Time of		End Date/Time of		Study Day of Start of		Study Day of End of	
Epoch		Treatment		Treatment		Treatment		Treatment	
Char		Char		Char		Num		Num	
50		50		50		8		8	
TREATMENT		2012-12-01		2012-12-01		2		-2	
TREATMENT		2012-12-02		2012-12-02		0		-3	
TREATMENT		2012-12-03		2012-12-03		-4		-4	
TREATMENT		2012-11-30		2012-11-30		-1		1	







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Executability

- Fully executable
- Partially executable
 - FDAB057: When collecting ethnicity demographic data from clinical trial participants, the following two minimum choices should be offered: "HISPANIC OR LATINO" or "NOT HISPANIC OR LATINO"
- Not executable
 - FDAB055: Trial participants should self-report race and ethnicity and they should not be assigned by the study team.
 - FDAB065: DS, CL, EG, EX, LB, MA, MI, PC, PP, and VS should be submitted if collected.





Progress



Status of the rules

- 48 new volunteers onboarded in February
- All rules specified by end of April







Next Steps



What's next

- Creating and testing all rules
- Providing unit test packages to FDA for reference
 - Positive and negative test data
 - YAML syntax and JSON code
 - Results
- FDA verification of published FDA Business Rules
- Specification of ADaM rules
- Testing by industry
- Adoption by the industry
- Ongoing maintenance following the governance process





Thank You!

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